UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

LASANDRA MADDEN Individually and on Behalf of LABREA WILLIAMS, a minor child, Plaintiffs,	§	
v. ORIGINAL	§	CIVIL ACTION NO. 3:03-CV-0167-BD
WYETH d/b/a WYETH, INC., f/k/a AMERICAN HOME PRODUCTS CORPORATION; WYETH CONSUMER HEALTHCARE, an unincorporated Division of WYETH, f/k/a WHITEHALL-ROBINS HEALTHCARE; AND WHITEHALL LABORATORIES, INC., Defendants.	§	

APPENDIX
PLAINTIFFS' REPLY TO DEFENDANT'S RESPONSE
TO PLAINTIFFS' MOTION FOR PARTIAL SUMMARY JUDGMENT

Item App. page

Vinson&Elkins

Beth Fancher bfancher@velaw.com
Tel 214.661.7314 **Fax** 214.661.4314

April 22, 2005

Mr. James C. Barber
Law Offices of James C. Barber
4310 Gaston Avenue
Dallas, TX 75246

Re: *LaSandra Madden, et al v. Wyeth, et al*; Cause No. 3-03CV-0167R, in the United States District Court, Northern District of Texas – Dallas Division

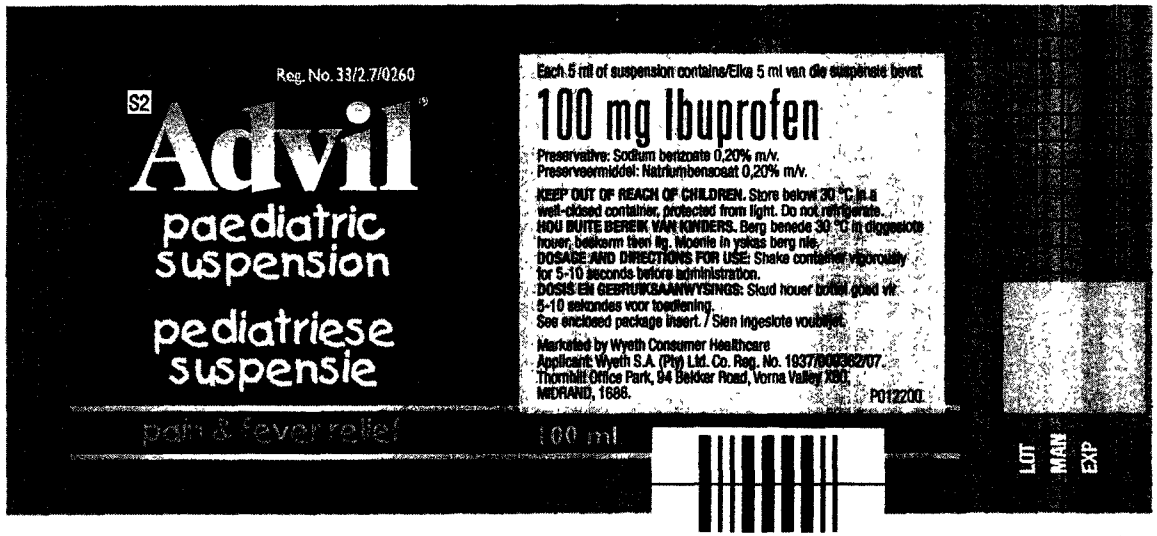
Dear Mr. Barber:

Enclosed are South African labels for Children's Advil, numbered W014785-14788. Also enclosed are documents numbered W014789-14806, which are current French labels and leaflets, as well as the labels, leaflets and SPC that will be implemented later this year. If you have any questions please do not hesitate to contact me.

Sincerely,

Beth Fancher
Paralegal

Enclosures



·GRAFFITI LTD·

Process Black	Pantone 314 CV	Pantone 2425 CV	Pantone 3135 CV	Cutter

Date: *12/11/02*	**Tints:**
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Client Ref: *P012200 TJW 075646*	*Graduated line either side of Pantone 2425 CV solid bar : 100% Pantone Yellow CV – 5% Pantone Yellow CV*
Job Name: *Advil Paediatric Suspension 100ml S.A.*	*Light coloured box containing the words "100mg Ibuprofen" : 40% Pantone Green 3135 CV*
Proof No: *Five*	*Grid in the background of the same box : 25% Pantone Green 3135 CV*
Our Ref: *026290*	*Area for Variable text overprinting : 25% Cutter*
Size: *138mm (W) x 55mm (H)*	*Overall Background : Solid Pantone 3135 CV*
Pharma Code: *827*	

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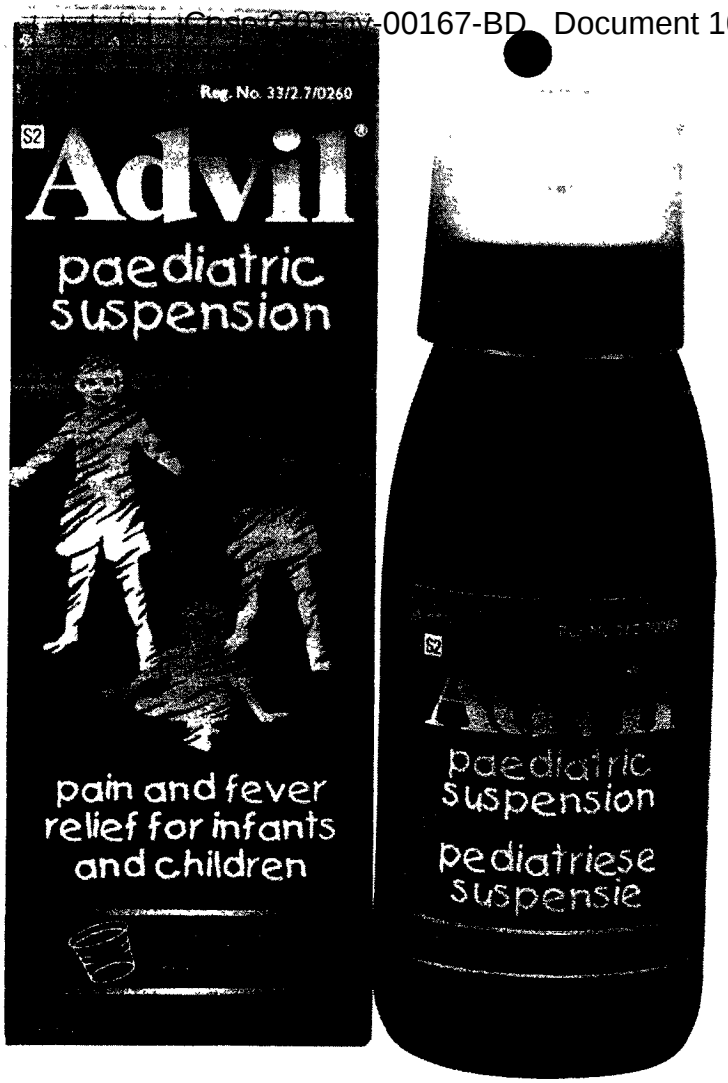
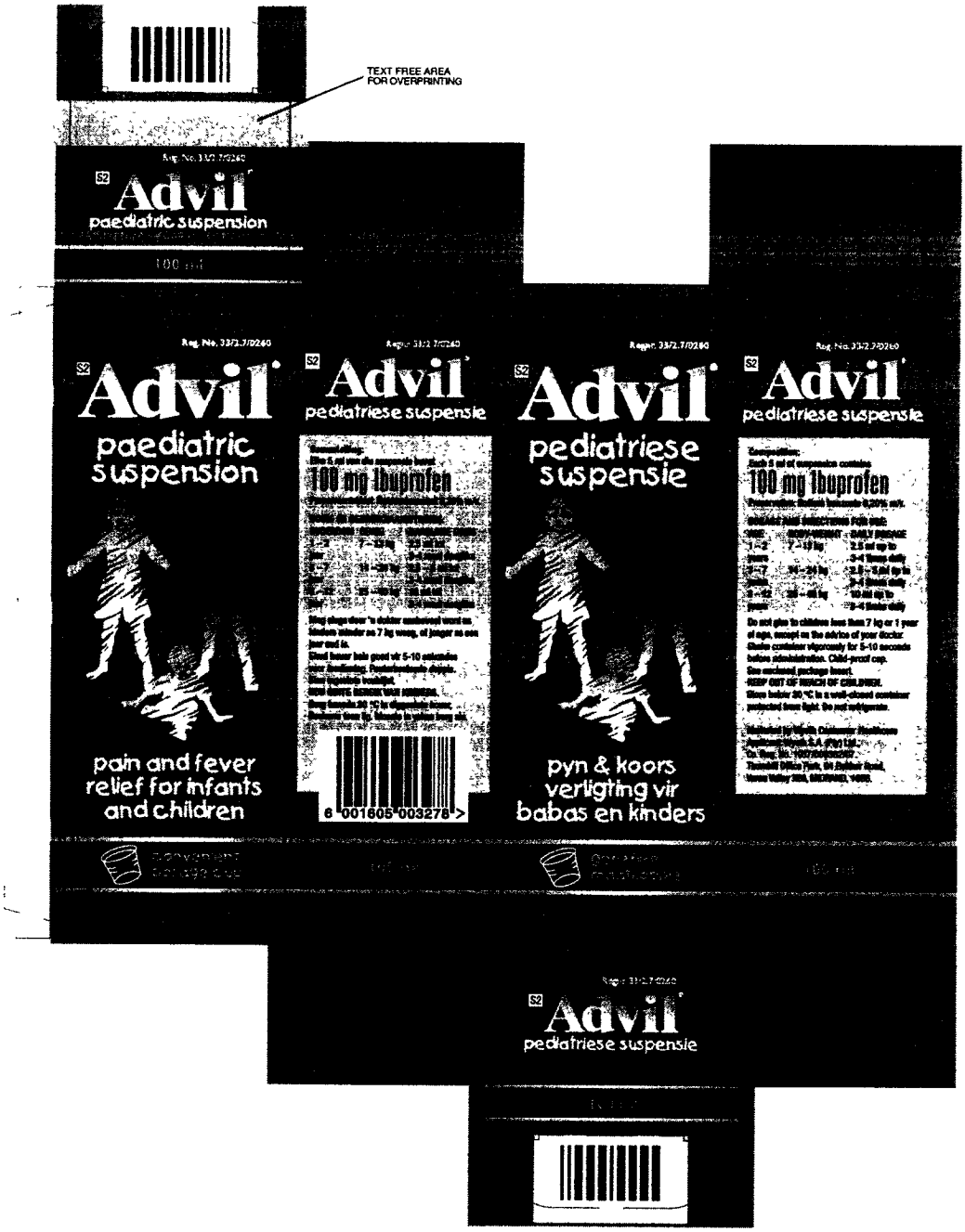

Reg. No. 33/2.7/0260
S2
Advil
paediatric suspension
pain and fever relief for infants and children
S2
paediatric suspension
pediatriese suspensie

W014786



·GRAFFITI LTD·

Date: 12/11/02	**Tints:**
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Client Ref: P012205 TJW075646	*Graduated line either side of Pantone 2425 CV solid bar : 100% Pantone Yellow CV – White*
Job Name: Advil Paed. Susp 100ml. SA. CARTON	*Light coloured box containing the words "100mg Ibuprofen" : 40% Pantone Green 3135 CV*
Proof No: Four	*Grid in the background of the same box : 25% Pantone Green 3135 CV*
Our Ref: 026289	*Area for Variable text overprinting : 20% Cutter*
CT: CT 24	*Overall Background : Solid Pantone 3135 CV*
Pharma Code: 1262	

Pantone 3135 CV | Cutter

The 'Cutter' has been coloured in red to make it easier to view on the 'blue' background.


Reg. No. 33/2.7/0250
S2
Advil®
paediatric suspension
pain and fever relief for infants and children
convenient dosage cup

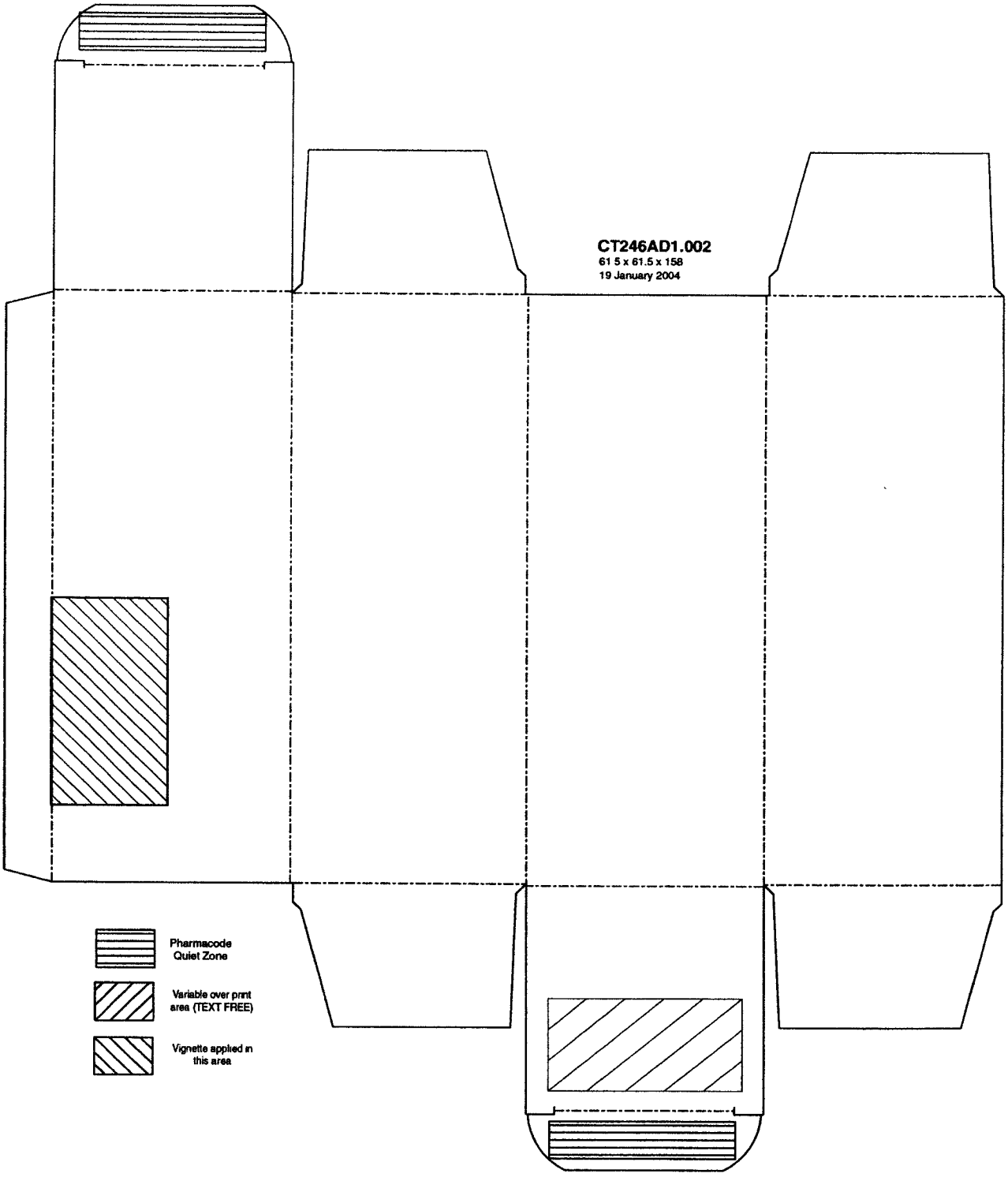
W014788

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy
PMS 280 Process Black Warm Red Dieline

W014789

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy

Dieline



W014790

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy
PMS 280

3364062

P012194
CT246

W014791

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy
Process Blue

W014792

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy
Process Yellow

Advil enfants & nourrissons 20mg/ml

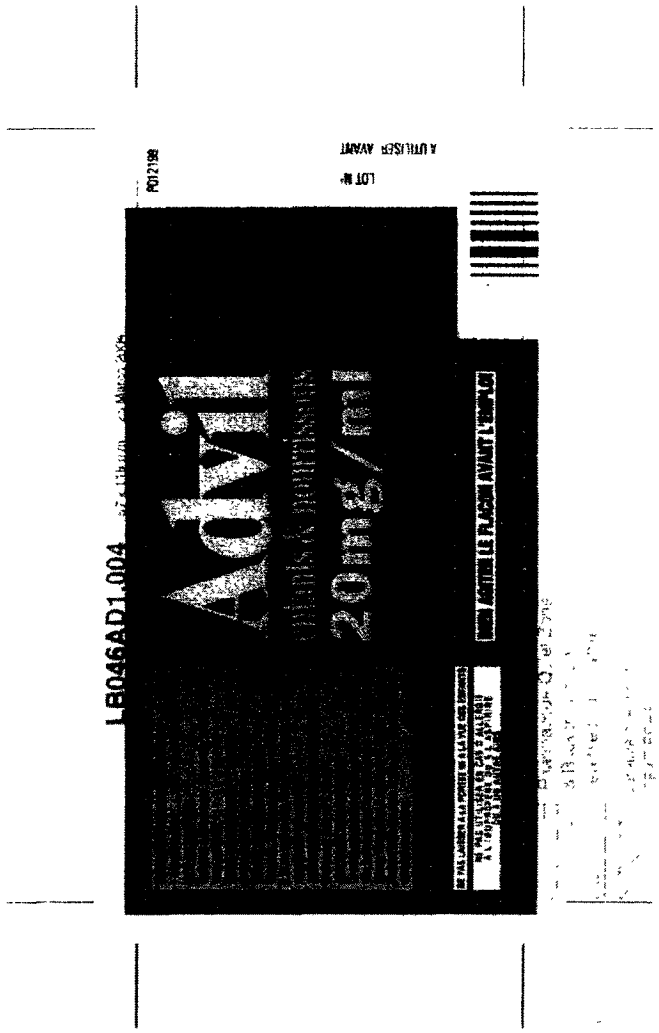
Advil enfants & nourrissons 20mg/ml
Advil enfants & nourrissons 20mg/ml
Advil enfants & nourrissons 20mg/ml

W014793

JOB-28049 Advil Children's Suspension 200 ml Carton - Havant for France 3P 2/09/04 zy
Warm Red

W014794

JOB-28600 Advil Paed SUSP, 200ml John Wyeth, Havant for France 2P 4.15.04 zy
LB046AD1.004 57 x 118mm
Process Blue PMS 280



W014795

JOB-29674 Advil Paed LP09 Havant for France 2P 9.2.04 lfd

Pharmacode 114

Black

LF004AP1.001

LF004AP1.001

Advil

enfants & nourrissons

20mg/ml

Suspension buvable en flacon

[illegible]

exceptionnellement, vertiges, maux de tête, rares troubles de la vue, diminution importante des urines, insuffisance rénale.

Dans tous les cas, il faut en avertir votre médecin.

Exceptionnellement, ont été observées des modifications du bilan hépatique ou de la formule sanguine (baisse des globules blancs ou des globules rouges) pouvant être graves.

SI VOUS REMARQUEZ DES EFFETS INDESIRABLES NON MENTIONNES DANS CETTE NOTICE, VEUILLEZ EN INFORMER VOTRE MEDECIN OU PHARMACIEN.

COMMENT CONSERVER ADVIL ENFANTS ET NOURRISSONS 20mg/ml, suspension buvable en flacon ?

Ce médicament est à conserver à une température comprise entre +4°C et +30°C.

Ne laisser ni à la portée ni à la vue des enfants.

Ne pas utiliser après la date de péremption figurant sur le flacon.

N'utilisez pas ADVIL ENFANTS ET NOURRISSONS 20mg/ml, suspension buvable en flacon, si vous constatez des signes visibles de détérioration.

La dernière date à laquelle cette notice a été révisée est juillet 2004

CONSEILS D'EDUCATION SANITAIRE

"QUE FAIRE EN CAS DE FIEVRE"

La température normale du corps est variable d'un individu à l'autre et comprise entre 36°5 et 37°5. Une élévation de plus de 0°8 peut être considérée comme une fièvre.

- Chez le nourrisson (moins de 2 ans).

La fièvre peut être dangereuse.

[illegible]

Ce qu'il faut faire :

[illegible]

WHITEHALL P012216

W014796

JOB-29673 Advil Paed LP10 Havant for France 2P 9.2.04 lfd

Pharmacode 106

Black

Advil

enfants & nourrissons

20mg/ml

Suspension buvable en flacon

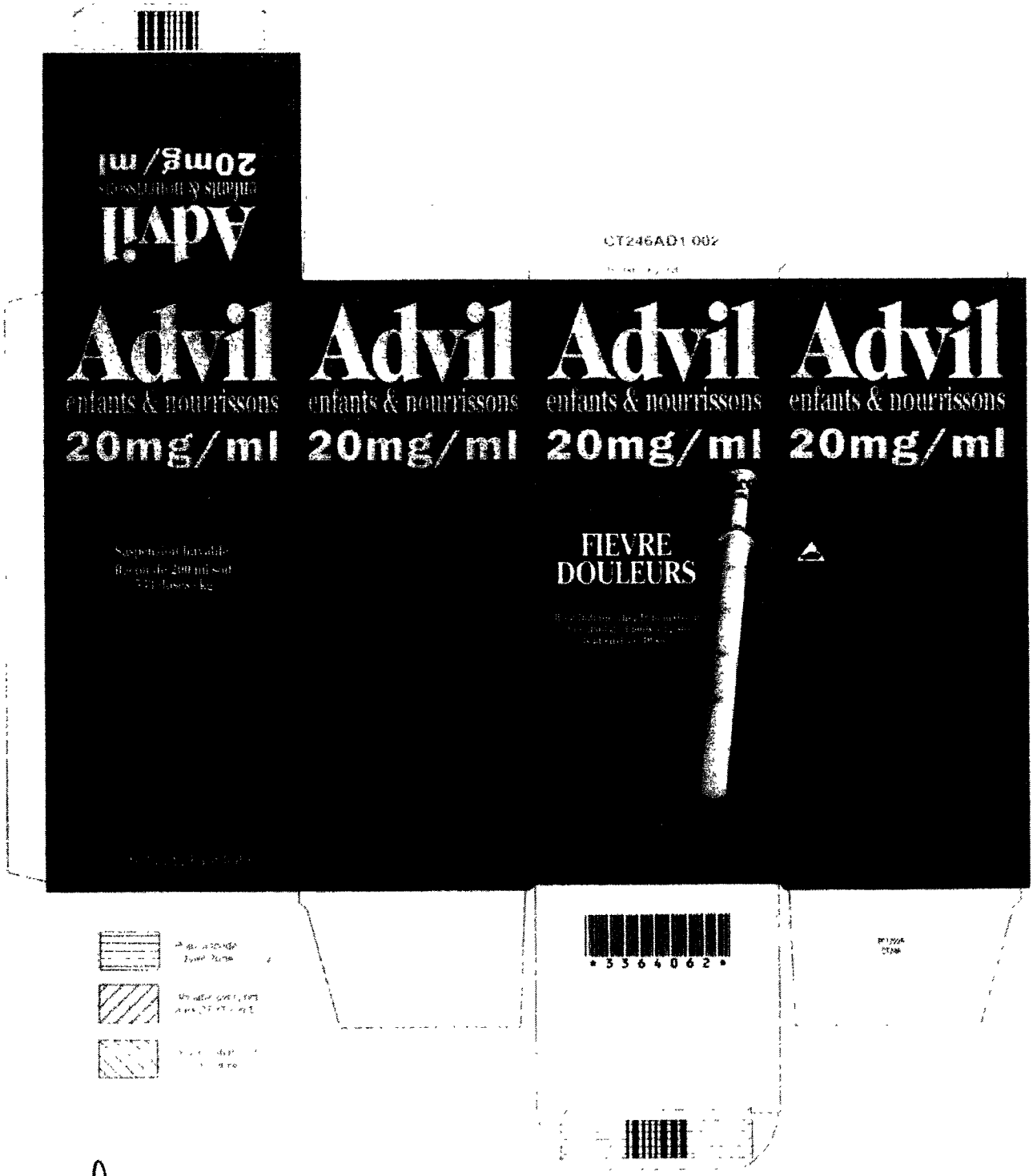
P012230

WHITEHALL

W014797

8/12/04

JOB-30058 Advil Paed Suspension 200 ml Carton - Havant for France 5P 12 7.04 eh
DWG: CT246AD1.002
PMS 280 Process Blue Warm Red

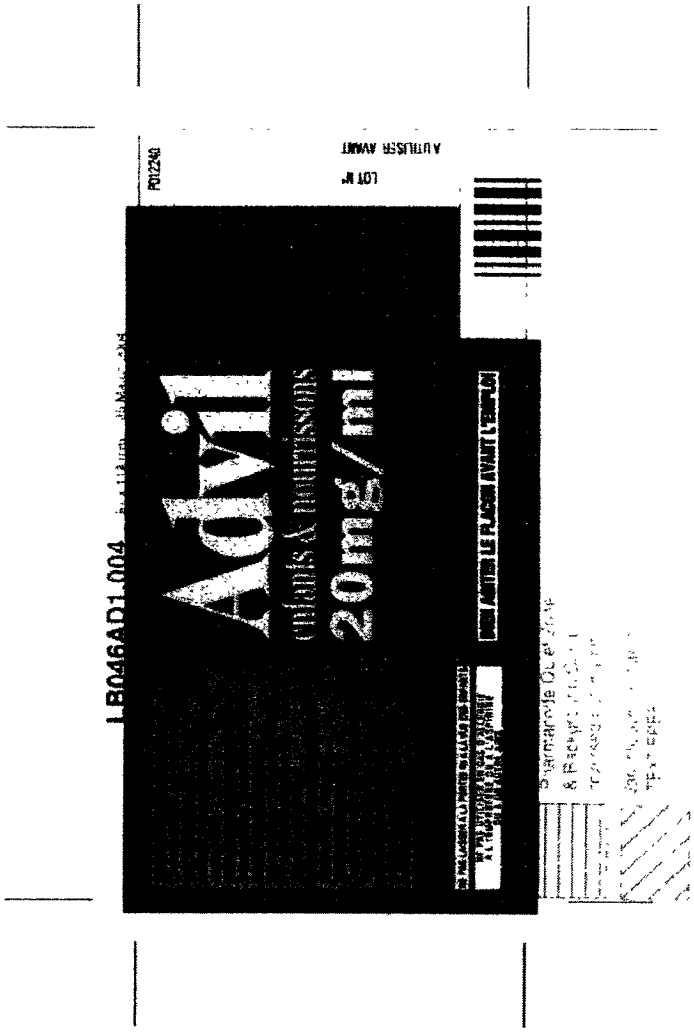


W014798

9 dec 04

02/12/2005

JOB-30057 Advil Paed SUSP, 200ml — John Wyeth, Havant for France 4P 12.1.04 eh
LB046AD1.004 57 x 118mm
Process Blue PMS 280



White bg adv cy.

W014799

Advil
enfants & nourrissons
20mg/ml
Suspension buvable en flacon

Lisez attentivement l'intégralité de cette notice avant de prendre ce médicament.
Elle contient des informations importantes sur votre traitement.
Si vous avez d'autres questions, si vous avez un doute, demandez plus d'informations à votre médecin ou à votre pharmacien.
Gardez cette notice, vous pourriez avoir besoin de la relire.
Si les symptômes s'aggravent ou persistent, consultez un médecin.

- La substance active est l'ibuprofène.
- Les autres composants sont du saccharose, du glycérol, du sorbitol à 70 pour cent (cristallisable), du polysorbate 80, du benzoate de sodium, de l'acide citrique anhydre, de l'édétate de sodium, de la gomme xanthane, de l'arôme fraise (contient de la vanilline), de l'arôme artificiel, de l'acésulfame de potassium, du rouge cochenille A et de l'eau purifiée.

Titulaire et Exploitant : Wyeth Santé Familiale, Cœur Défense, Tour A, La Défense 4, 92931 Paris La Défense Cédex - France
Fabricant : WYETH Laboratories, New Lane, HAVANT, HANTS PO9 2NG, Grande Bretagne

QU'EST-CE QUE ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon ET DANS QUELS CAS EST-IL UTILISE ?
Suspension buvable, flacon de 200 ml.
ANTIINFLAMMATOIRE ET ANTIRHUMATISMAUX NON STEROIDIENS
Ce médicament contient de l'ibuprofène. Il est indiqué, chez le nourrisson et l'enfant de 3 mois à 12 ans (soit environ 40 kg), dans le traitement de la fièvre et/ou des douleurs telles que :
- maux de tête,
- états grippaux,
- douleurs dentaires,
- courbatures.

INFORMATIONS NECESSAIRES AVANT D'UTILISER ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon.
Ne pas utiliser ce médicament dans les cas suivants :
- au-delà de 5 mois de grossesse révolus (24 semaines d'aménorrhée),
- antécédent d'allergie ou d'asthme déclenché par la prise de ce médicament ou d'un médicament apparenté, notamment autres anti-inflammatoires non stéroïdiens, aspirine,
- antécédents d'allergie à l'un des constituants de ce produit,
- ulcère de l'estomac ou du duodénum en évolution,
- maladie grave du foie,
- maladie grave des reins,
- maladie grave du cœur,
- lupus érythémateux disséminé.

Prendre des précautions particulières avec ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon :
En cas de douleurs et/ou de fièvre, ne pas dépasser la dose maximale de 30 mg/kg/jour. En effet, à ces doses, ce médicament peut provoquer des inconvénients parfois graves, qui sont peux observés avec les médicaments anti-inflammatoires.
AVANT D'UTILISER CE MEDICAMENT, CONSULTER VOTRE MEDECIN, EN CAS :
- d'antécédent d'asthme associé à une rhinite chronique, une sinusite chronique ou des polypes dans le nez. L'administration de cette spécialité peut entraîner une crise d'asthme, notamment chez certains sujets allergiques à l'aspirine ou à un anti-inflammatoire non stéroïdien (cf. contre-indications),
- de traitement anticoagulant concomitant. Ce médicament peut entraîner des manifestations gastro-intestinales graves.
- d'antécédents digestifs (hernie hiatale, hémorragie digestive, ulcère de l'estomac ou du duodénum anciens),
- de maladie du cœur, du foie ou du rein,
- de varicelle. Ce médicament est déconseillé en raison d'exceptionnelles infections graves de la peau,
- d'intolérance au fructose, de syndrome de malabsorption du glucose et du galactose ou de déficit en sucrase-isomaltase (maladies métaboliques rares). Ce médicament ne doit pas être utilisé en raison de la présence de saccharose et de sorbitol,

AU COURS DU TRAITEMENT :
- en cas de troubles de la vue, PREVENIR VOTRE MEDECIN,
- en cas d'hémorragie gastro-intestinale, ARRETER LE TRAITEMENT ET CONTACTER IMMEDIATEMENT UN MEDECIN OU UN SERVICE MEDICAL D'URGENCE.
- d'apparitions de signes cutanés ou muqueux qui ressemblent à une brûlure (rougeur avec bulles ou cloques, ulcérations), ARRETEZ LE TRAITEMENT ET CONTACTEZ IMMEDIATEMENT UN MEDECIN OU UN SERVICE MEDICAL D'URGENCE,
- en cas de signes évocateurs d'allergie à ce médicament, notamment crise d'asthme ou brusque gonflement du visage et du cou (cf. quels sont les effets indésirables éventuels ?), ARRETEZ LE TRAITEMENT ET CONTACTEZ IMMEDIATEMENT UN MEDECIN OU UN SERVICE MEDICAL D'URGENCE.

Ce médicament contient un anti-inflammatoire non stéroïdien : l'ibuprofène.
Votre enfant ne doit pas prendre en même temps que ce médicament d'autres médicaments contenant des anti-inflammatoires non stéroïdiens et/ou de l'aspirine.
Lisez attentivement la notice des autres médicaments que prend l'enfant afin de vous assurer de l'absence d'anti-inflammatoires non stéroïdiens et/ou d'aspirine.

En cas de diabète ou de régime hypoglucidique (pauvre en sucre), tenir compte de la teneur en saccharose (0,5 g par ml).

Grossesse
Ce médicament est destiné au nourrisson et à l'enfant. Cependant, en cas d'utilisation dans des circonstances exceptionnelles par une femme susceptible d'être enceinte, il faut rappeler les faits suivants :
Au cours du premier trimestre de grossesse (12 semaines d'aménorrhée soit 12 semaines après le 1er jour de vos dernières règles), votre médecin peut être amené, si nécessaire, à vous prescrire ce médicamment.
De 2,5 à 5 mois de grossesse révolus (12 à 24 semaines d'aménorrhée), ce médicament ne sera utilisé que sur les conseils de votre médecin et en prise brève. L'utilisation prolongée de ce médicament est fortement déconseillée
Au-delà de 5 mois de grossesse révolus (au-delà de 24 semaines d'aménorrhée), vous ne devez EN AUCUN CAS prendre ce médicament, car ses effets sur votre enfant peuvent avoir des conséquences graves notamment sur un plan cardio-pulmonaire et rénal, et cela même avec une seule prise.
Si vous avez pris ce médicamnet alors que vous étiez enceinte de plus de cinq mois révolus, parlez en à votre gynécologue obstétricien afin qu'une surveillance adaptée vous soit proposée.
Demandez conseil à votre médecin ou à votre pharmacien avant de prendre tout médicament.

Allaitement
Ce médicament passe dans le lait maternel. Par mesure de précaution, il convient d'éviter de l'utiliser pendant l'allaitement.
Demandez conseil à votre médecin ou à votre pharmacien avant de prendre tout médicament.

Conduite de véhicules et utilisation de machines :
Dans de rares cas, la prise de ce médicament peut entraîner des vertiges et des troubles de la vue.

Liste des excipients à effet notoire :
Saccharose, glycérol, sorbitol, rouge cochenille A.

Prise ou utilisation d'autres médicaments :
Veuillez indiquer à votre médecin ou à votre pharmacien si votre enfant a pris récemment un autre médicament, notamment des anticoagulants oraux, d'autres anti-inflammatoires non stéroïdiens y compris l'aspirine et ses dérivés, de l'héparine, du lithium, du méthotrexate à fortes doses (supérieures à 15 mg par semaine), même s'il s'agit d'un médicament obtenu sans ordonnance.

COMMENT UTILISER ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon ?
Réservé au nourrisson et à l'enfant, de 3 mois à 12 ans (soit environ 40 kg).
La posologie usuelle est de 20 à 30 mg/kg/jour en 3 à 4 prises sans dépasser 30 mg/kg/jour. Le médicament s'administre au moyen de la seringue pour administration orale (graduée en kg) qui délivre une dose de 7,5 mg/kg par prise. La dose à administrer pour 1 prise est obtenue en aspirant la suspension en tirant le piston de la seringue pour administration orale jusqu'à la graduation correspondant au poids de l'enfant.
Pour chaque prise :
- jusqu'à 25 kg : remplir la seringue jusqu'à la graduation indiquant le poids de l'enfant.
  entre 25 kg et 40 kg : remplir une première fois la seringue jusqu'à la graduation 25 kg puis une deuxième fois jusqu'à atteindre un total égal au poids de l'enfant (exemple pour un enfant de 30 kg : remplir une première fois la seringue jusqu'à la graduation 25 kg puis une deuxième fois jusqu'à la graduation 5 kg).
- au-delà de 40 kg : il existe des formes pharmaceutiques plus adaptées.

Voie orale.
Bien agiter le flacon avant l'emploi.
Faire boire de l'eau après absorption de la suspension.
Les prises systématiques permettent d'éviter les oscillations de douleur ou de fièvre. Elles doivent être espacées d'au moins 6 heures.
Durée du traitement : si la douleur persiste plus de 5 jours ou la fièvre plus de 3 jours, ou si elles s'aggravent ou en cas de survenue d'un nouveau trouble, en informer votre médecin.
Si vous avez donné plus d'ADVIL ENFANTS ET NOURRISSONS 20 mg/ml suspension buvable en flacon que vous n'auriez dû, consultez immédiatement votre médecin ou votre pharmacien.
Si vous oubliez de donner ADVIL ENFANTS ET NOURRISSONS 20 mg/ml suspension buvable en flacon : ne donnez pas de dose double pour compenser la dose simple que vous avez oubliée de donner.

QUELS SONT LES EFFETS INDESIRABLES EVENTUELS ?
Comme tout médicament, ADVIL ENFANTS ET NOURRISSONS 20 mg/ml suspension buvable en flacon est susceptible d'entraîner des effets indésirables.
La prise de ce médicament peut entraîner une sensation de picotement dans la bouche et/ou dans la gorge : faire boire de l'eau.
- Peuvent survenir des réactions allergiques :
  - cutanées : éruption sur la peau, allergie cutanée, démangeaisons, œdème, aggravation d'urticaire chronique,
  - respiratoires : crise d'asthme,
  - généralisées : brusque gonflement du visage et du cou (œdème de Quincke)
- Dans certains cas rares, il est possible que survienne une hémorragie digestive (rejet de sang par la bouche ou dans les selles, coloration des selles en noir). Celle-ci est d'autant plus fréquente que la posologie utilisée est élevée.
- Il peut exceptionnellement être observé des maux de tête accompagnés de nausées, de vomissements et de raideur de la nuque.
- Exceptionnellement, des infections graves de la peau ont été observées en cas de varicelle.
- Très exceptionnellement peuvent survenir des manifestations bulleuses de la peau ou des muqueuses (sensation de brûlure accompagnée de rougeur avec bulles, cloques, ulcérations).

Dans tous ces cas, il faut immédiatement arrêter le traitement et avertir votre médecin.
- Au cours du traitement, il est possible que surviennent :
  - des troubles digestifs : maux d'estomac, vomissements, nausées, diarrhée, constipation,
  - exceptionnels vertiges ou maux de tête, rares troubles de la vue, diminution importante des urines, insuffisance rénale.

Dans tous les cas, il faut en avertir votre médecin.
Exceptionnellement, ont été observées des modifications du bilan hépatique ou de la formule sanguine (baisse des globules blancs ou des globules rouges) pouvant être graves.
Si vous remarquez des effets indésirables non mentionnés dans cette notice, veuillez en informer votre médecin ou pharmacien.

COMMENT CONSERVER ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon ?
Ce médicament est à conserver à une température comprise entre + 4°C et + 30°C.
Ne laisser ni à la portée ni à la vue des enfants.
Ne pas utiliser après la date de péremption figurant sur le flacon.
N'utilisez pas votre flacon d'ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, suspension buvable en flacon, si vous constatez des signes visibles de détérioration.
La dernière date à laquelle cette notice a été révisée est février 2005

CONSEILS D'EDUCATION SANITAIRE
- «QUE FAIRE EN CAS DE FIEVRE»
La température normale du corps est variable d'un individu à l'autre et comprise entre 36°5 et 37°5. Une élévation de plus de 0°8 peut être considérée comme une fièvre.
- **Chez le nourrisson (moins de 2 ans) :**

La fièvre peut être dangereuse :
- elle entraîne un risque de convulsion si elle monte trop et surtout trop vite,
- elle entraîne un risque de déshydratation.

Ce qu'il faut faire :
- déshabiller l'enfant (un enfant nu dans une pièce à 20°C ne risque rien),
- lui présenter souvent à boire (certains enfants boivent très peu mais très souvent),
- lui faire prendre un médicament contre la fièvre, après s'être assuré que le médicament est adapté au poids du nourrisson, en respectant les doses indiquées.

Ce qu'il ne faut pas faire :
- couvrir l'enfant, ce qui augmente le risque de convulsion et de déshydratation,
- le mettre «à la diète».

Consultez un médecin :
Dans les heures qui suivent, si la température est élevée à plus de 38°5 et si elle est accompagnée d'autres anomalies : comportement inhabituel (cris, pleurs, somnolence), vomissement, diarrhée.
- **Chez l'enfant de plus de 2 ans :**

Si les troubles qu'elle entraîne sont trop gênants, vous pouvez donner un médicament contre la fièvre, après s'être assuré que le médicament est adapté au poids de l'enfant, en respectant les doses indiquées.
Néanmoins :
- si d'autres signes apparaissent (comme une éruption cutanée) ou si la température persiste plus de 3 jours ou si elle s'aggrave, consultez un médecin,
- si les maux de tête deviennent violents, en cas de vomissements, **consultez immédiatement un médecin.**

«QUE FAIRE EN CAS DE DOULEURS»
Consultez un médecin :
- En l'absence d'amélioration au bout de 5 jours de traitement.
- Si les douleurs reviennent régulièrement.
  Si elles s'accompagnent de fièvre,
  Si elles vous réveillent votre enfant la nuit.

Wyeth Santé Familiale

le 15/2/05

APPENDIX I

SUMMARY OF PRODUCT CHARACTERISTICS

Corrected & modified on Feb 9th, 2005

1. NAME OF MEDICINAL PRODUCT

ADVIL ENFANTS ET NOURRISSONS 20 mg/ml, oral suspension in vial.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen ..... 20.00 mg

For 1 ml oral suspension

A graduated mark of 1 kg corresponds to 0.375 ml of oral suspension and contains 7.5mg ibuprofen.

3. PHARMACEUTICAL FORM

Oral suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Symptomatic therapy of painful disorders and/or febrile conditions.

4.2 Posology and Method of Administration

For children and infants use only, from 3 months to 12 years of age (i.e., approximately 40kg).
Oral route.

Shake well before use.
Have the child or infant drink water after ingestion of the solution.

Posology:

The usual posology is 20-30 mg/kg/day in 3-4 divided doses, without exceeding 30 mg/kg/day.
The medication is administered orally using a syringe (graduated in kg) which delivers a 7.5 mg/kg dose per administration.
To obtain 1 dose for administration, draw in the suspension by pulling on the plunger of the oral administration syringe to the graduated mark which corresponds to the child's weight.

For each dose:
- up to 25 kg: fill the graduated syringe to the mark corresponding to the child's weight;
- between 25 and 40 kg: fill the syringe once to the 25 kg graduated mark, then a second time to the graduated mark necessary to reach the total weight of the child (example for a child of 30 kg: fill the syringe once to the 25 kg graduated mark, then a second time to the 5 kg graduated mark);
- beyond 40 kg (i.e., around 12 years old): better suited pharmaceutical forms are available.

Frequency of Administration:

Systematic ingestion of doses makes it possible to prevent fluctuations of pain or fever. Doses should be taken at least at 6-hour intervals.

4.3 Contraindications

This medicinal product is contraindicated in the following cases:
- starting with 24 weeks of amenorrhea (end of month 5 of pregnancy) (see Pregnancy and Lactation);
- in case of a previous history of allergy or asthma triggered by ingestion of ibuprofen or substances with similar activity such as other NSAIDs or aspirin;
- previous history of allergy to other ingredients in the suspension;
- active gastro-duodenal ulcer;
- severe hepato-cellular insufficiency;
- severe impaired renal function;
- severe heart failure, not controlled;
- systemic lupus erythematosus.

4.4 Special Warnings and Special Precautions for Use

Patients presenting with asthma in combination with chronic rhinitis, chronic sinusitis and/or nasal polyposis are at risk of allergic manifestations when taking aspirin and/or a non-steroidal anti-inflammatory drug. Administration of the medicinal product can result in an asthma attack, in particular in certain subjects who are allergic to aspirin or an NSAID (see Contraindications).

Gastro-intestinal bleeding or ulcer/perforation can occur at any time during treatment without premonitory symptoms or a previous history of such disorders necessarily being observed.. The relative risk increase in the elderly, in patients in a debilitated condition, patients with low body weight, and patients receiving anticoagulant or platelet-inhibiting agents (see Interactions with Other Medicaments and Other Forms of Interactions). In case of gastro-intestinal bleeding or ulcer, this treatment should immediately be discontinued.

Chicken pox can in rare cases be the origin of serious complications of cutaneous and soft tissue infections. To date, the role favoring the NSAIDs on the aggravation of these infections cannot be disregarded. It is then, prudent to avoid the use of Advil in the case of chicken pox.

Severe cutaneous reactions and life-threatening allergies may occurred with all NSAID. Ibuprofen must be withdrawn in case of cutaneous and mucous side effect.

ANNEX III B- 9th Feb 2005

PACKAGE LEAFLET

Read all of this leaflet carefully before you start taking this medicine.
It contains important information on your treatment
If you have further questions, please ask your doctor or your pharmacist.
Keep this leaflet, you may need to read it again.
You must see a doctor if your symptoms worsen or do not improve.

ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle.

- Active substance is IBUPROFEN
- Other ingredients are: Sucrose, glycerol, 70% Sorbitol (crystallized), polysorbate 80, sodium benzoate, anhydrous citric acid, edetate sodium, xantham gum, strawberry flavor (containing vanillin), artificial flavor, acesulfame potassium, red iron oxide, purified water.

Marketing Authorization Holder / Distributor:

WYETH SANTE FAMILIALE
Cœur Défense – Tour A
La Défense 4
110, Esplanade du Général de Gaulle
92931 Paris la Défense Cedex

Manufacturer:

WYETH MANUFACTURING
New Lane, Havant
Hants P09 2NG
UK

1. WHAT IS ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle, AND WHAT IT IS USED FOR?

Oral suspension in 200 ml bottle
This medication contains a non-steroidal anti-inflammatory agent: ibuprofen. It is indicated in children and infants from 3 months to 12 years of age (i.e approximately 40 kg), for treatment of fever and/or pain such as headache, flu-like illness, toothache, muscle stiffness.

2. BEFORE YOU TAKE ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle

Do not take this medicine in the following cases:

- starting with 24 weeks of amenorrhea (end of month 5 of pregnancy) (see Pregnancy and Lactation);
- previous history of allergy or asthma triggered by ingestion of this medication or a similar medication, in particular other non-steroidal anti-inflammatory agents or aspirin.
- previous history of allergy to one of the product's excipients,
- active gastric or duodenal ulcer,
- serious liver disease,
- serious kidney disease,
- serious heart disease,
- systemic lupus erythematosus,

Take special care with **ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle**:

In case of pain and/or fever, do not exceed the maximum dose of 30 mg/kg/day. Indeed, at these doses, this medicinal product may cause sometimes serious undesirable effects which are those observed with other anti-inflammatory agents.

BEFORE USING THIS MEDICATION, TELL YOUR DOCTOR IN CASE OF THE FOLLOWING CASES :

- History of asthma associated to chronic rhinitis, chronic sinusitis, or nasal polyps. Administration of this medicinal product may cause an acute attack of asthma notably in some subjects allergic to aspirin or to a non-steroidal anti-inflammatory agent (see contraindications).
- Concomitant anti-coagulant therapy. This medication may cause serious gastrointestinal reactions.
- History of GI disorders (hiatal hernia, GI bleeding, previously known ulcer of the stomach or of the duodenum),
- Heart, liver or kidney disease,
- Chicken pox. This medication is not recommended because of rare serious dermatological infections,
- Intolerance to fructose, a glucose malabsorption syndrome or a sucrose-isomaltase deficiency (rare metabolic disorders), because of the presence of sucrose and sorbitol.

DURING TREATMENT:

- If visual disorders occur, INFORM YOUR DOCTOR,
- In case of gastrointestinal bleeding, DISCONTINUE TREATMENT AND IMMEDIATELY CONTACT A DOCTOR OR AN EMERGENCY MEDICAL SERVICE.
- In case of apparition of cutaneous or mucous signs which look like burns (redness of the skin associated to bullous, blister or ulceration), DISCONTINUE TREATMENT AND IMMEDIATELY CONTACT A DOCTOR OR AN EMERGENCY MEDICAL SERVICE.
- In case of signs of allergy, i.e asthma episode or sudden swelling of the face and neck (see 4.Possible side effects), DISCONTINUE TREATMENT AND IMMEDIATELY CONTACT A DOCTOR OR AN EMERGENCY MEDICAL SERVICE.

In case of diabetes or low-sugar diet, sucrose content (0.5g per ml) should be taken into account.

This medication contains a non-steroidal anti-inflammatory agent, Ibuprofen
Your child should not take this medicinal product at the same time as other medicinal products which contain a non-steroidal anti-inflammatory agent and/or aspirin.
Carefully read the leaflet for other medicinal products that your child is taking to make certain of the absence of non-steroidal anti-inflammatory agents and/or aspirin.

Pregnancy

This medicinal product is intended for infants and children. However, in the case of use in rare situations in women of childbearing age, the following should be kept in mind:

- **During the 1st trimester of pregnancy** (12 weeks of amenorrhea), your doctor could, if necessary, give you this medication.

- **From 2.5 to 5 months of pregnancy** (12 to 24 weeks of amenorrhea), this medicinal product will be used only based on a doctor's advice, and during short periods of times.

- **After 5 months of pregnancy** (after 24 weeks of amenorrhea), you should NOT IN ANY CASE take this medication as it can have serious consequences on your unborn child, in particular cardiopulmonary and renal side effects and even at a single dose. If you have taken this medication after 5 months of pregnancy, you should ask your doctor to get an appropriate follow-up.

Ask your doctor or pharmacist's advice before taking any medication.

Breastfeeding

This medication is excreted in human breast milk, as a precautionary measure, it is necessary to avoid administering it to a breast-feeding woman.

Ask your doctor or pharmacist's advice before taking any medication.

Driving and using machines:
In rare cases, ingestion of this medicinal product may cause dizziness and visual disorders.

List of excipients which have a noteworthy effect: sucrose, glycerol, sorbitol, red iron oxide.

Ingestion or use of other medications:
Tell your doctor or pharmacist if your child is taking or has recently taken another medicinal product, in particular all oral anticoagulants, all non-steroidal anti-inflammatory agent including high-dose salicylates, heparin, lithium, methotrexate (at doses greater than 15 mg/week), *even if it is a medication obtained without a doctor's prescription.*

3. HOW TO USE ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle ?

Reserved for infants and children from 3 months to 12 years of age (i.e approximately 40 kg).

The usual posology is 20-30 mg/kg/day in 3-4 divided doses, without exceeding 30 mg/kg/day.

The medication is administered orally using a syringe (graduated in kg) which delivers a 7.5 mg/kg dose per administration.
To obtain 1 dose for administration, draw in the suspension by pulling on the plunger of the oral administration syringe to the graduated mark which corresponds to the child's weight.

For each dose:
- up to 25 kg: fill the graduated syringe to the mark corresponding to the child's weight;
- between 25 and 40 kg: fill the syringe once to the 25 kg graduated mark, then a second time to the graduated mark necessary to reach the total weight of the child (example for a child of 30 kg: fill the syringe once to the 25 kg graduated mark, then a second time to the 5 kg graduated mark);
- beyond 40 kg (i.e., around 12 years old): better suited pharmaceutical forms are available.

Oral route.
Shake well before use.
Have the child or infant drink water after ingestion of the solution.

Systematic ingestion of doses makes it possible to prevent fluctuations of pain or fever. Doses should be taken at least at 6-hour intervals.

Duration of treatment: if pain lasts more than 5 days or fever more than 3 days, if they worsen or a new disorder appears, inform your doctor.

If you take more **ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle than you should:** immediately consult your doctor or pharmacist.

If you forget to take **ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle**: Do not take a double dose to make up for forgotten individual doses.

Effects when treatment with **ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle** is stopped: ***not applicable.***

4. POSSIBLE SIDE EFFECTS

Like all medicines, ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle *can have side effects:*

The following allergic reactions can occur:
- Cutaneous: skin eruptions, skin allergy, itching, edema, worsening of chronic urticaria.
- Respiratory: acute attack of asthma.
- Systemic: a type of urticaria with sudden swelling of the face and neck (angioedema).

In some rare instances, GI bleeding may occur (expulsion of blood by the mouth, in the stool, or a dark coloring of the stool). This is all the more common when dosage used is high.

Exceptionally, headache can be observed with nausea, vomiting and neck stiffness.

Exceptionally, serious dermatological infections have been observed during chicken pox.

Very exceptionally, bullous symptoms of the skin or mucosa (burning sensation associated to a redness of the skin with bullous, blister or ulceration).

In any case, you should immediately discontinue treatment and inform your doctor.

- During treatment, the following can occur:
  - GI disorders: stomach ache, vomiting, nausea, vomiting, diarrhea, constipation,
  - Other possible undesirable effects related to the medicinal product: in rare cases, dizziness, headache, visual disorders, major decrease in urine output, renal insufficiency.

In all cases, tell your doctor.

- Exceptionally, modification of liver function test or modification of blood count (decreasen of white cells or decrease of red cells) which can be serious may occur.

TELL YOUR DOCTOR OR PHARMACIST OF ANY UNDESIRABLE OR BOTHERSOME EFFECT NOT MENTIONED IN THIS LEAFLET.

5. STORING ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle

This medication should be stored at temperatures between +4 and +30°C.

Keep out of the reach and sight of children

Do not use after the expiry date stated on the carton.
Do not use ADVIL ENFANTS ET NOURRISSONS 20mg/ml, oral suspension in bottle if you notice visible signs of its deterioration.

This leaflet was last approved on {date}

6. HEALTH EDUCATION ADVICE

.....

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA

SUPPLEMENTAL LABELING REQUEST - CBE

Company
Attention:

Dear,

Please refer to your new drug application(s) (NDA) approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act DRUG NAME, STRENGTH, FORM FOR (EACH NDA NUMBER).

We additionally refer to the February 16-18, 2005 joint meeting of the Arthritis and Drug Safety and Risk Management Advisory Committees to discuss the overall benefit to risk considerations (including cardiovascular (CV) and gastrointestinal (GI) safety concerns) of COX-2 selective and non-selective, non-steroidal anti-inflammatory drugs (NSAIDs) and related agents.

We also refer to FDA's letter dated April 7, 2005, requesting cardiovascular information regarding your drug.

Consistent with recommendations made by the committee members, and following a thorough review of all available data, we believe that labeling changes are warranted to include more specific information for consumers, family members, and caregivers about potential risks of CV and GI adverse effects associated with the use of non-prescription NSAIDs (excluding aspirin). For additional information, please see www.fda.gov/cder/drug/infopage/cox2/default.htm. On this page you can find links to a number of relevant documents including the decision memo entitled "Analysis and Recommendations for Agency Action - COX-2 Selective and Non-selective NSAIDS."

Therefore, we request that you revise the labeling for all of your over-the-counter (OTC) products that contain any of the following ingredients: ibuprofen, ketoprofen, or naproxen. We request that you revise your labeling as specified in the enclosed templates and that the revisions be made for all OTC adult and pediatric drug products that contain these ingredients. We include adult warnings on the pediatric products in this request because such products are sometimes used by adults who cannot take solid oral dosage forms. For that reason, on our own initiative, we are also granting an exemption under 21 C.F.R. § 201.66 (e) to replace the word "you" with the word "user" in the standard headings in 21 C.F.R. § 201.66 (c)(5)(iv) and (v) so that the revised headings read "Ask a doctor before use if the user has" and "Ask a doctor or pharmacist before use if the user is" to accommodate the warning language specified in the template for children. We intend to propose to codify this change to 21 C.F.R § 201.66 (c) in a future amendment to the rulemaking, at which time you will have an opportunity to comment on this language.

In addition, we request that you revise the "Allergy alert" and "Alcohol warning" for all of your OTC products that contain ibuprofen, ketoprofen or naproxen as specified in the enclosed templates. The "Allergy alert" for these products should be revised to include a warning for aspirin sensitive individuals and a description of early symptoms associated with Stevens-Johnson Syndrome (SJS). The "Alcohol warning" currently required by 21 C.F.R. § 201.322 should also be relocated to appear as part of the new stomach bleeding warning.

In addition to the revision of the Drug Facts label, we also request that the Principal Display Panel (PDP) for all of the above-described products display the word "NSAID" in parentheses following the name of the NSAID ingredient. The word "(NSAID)" should appear highlighted in either fluorescent or color contrast or in bold type. The size should be at least one-half as large as the size of the most prominent printed matter on the PDP. For 12 months after introduction into the OTC marketplace, please also add to the PDP the statement "See new warnings information". This statement should also be highlighted in either fluorescent or color contrast or in bold type and the size should be at least one-third the size of the most prominent printed matter on the PDP.

Attached are templates that we request you to follow in preparing new labeling:

1. Template Drug Facts label for all adult products
2. Template Drug Facts label for pediatric ibuprofen-containing products
3. Template for the Principal Display Panel

In addition to the above recommended language, the Drug Facts label must incorporate all previous revisions that were agreed upon in your most recently approved labeling. Also, notwithstanding the specific format changes we request above with respect to 21 C.F.R. § 201.66 (c)(iv) and (v), your labeling must otherwise be formatted in accordance with the requirements of 21 C.F.R. § 201.66.

We remind you that if you have a package insert, it should also be changed to reflect the above revisions.

These labeling revisions should be submitted to FDA in the form of a "Supplement – Changes Being Effected" within 30 days from the date of this letter in accordance with the requirements of 21 C.F.R. § 314.70. Color-mock up labeling can be submitted in lieu of final printed labeling. If you deviate from the attached templates you must submit a prior approval supplement for our review and comment.

The labeling changes should be implemented within 6 months. If you are unable to meet this deadline, contact us to discuss the timing of your new labeling.

If you have any questions, call Laura Shay, Regulatory Project Manager, at 301-827-2274.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, M.D., M.P.H.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

Attachments:

1. Template Drug Facts label for all adult products
2. Template Drug Facts label for pediatric ibuprofen-containing product
3. Template for the Principal Display Panel

ADULT DRUG FACTS LABEL:

Drug Facts
Active ingredient (in each [insert dosage unit]) ***Purpose*** [*insert* active ingredient] XXX mg (NSAID)*.....Pain reliever/fever reducer * nonsteroidal anti-inflammatory drug
Uses • [add NDA approved uses]
Warnings **Allergy alert:** [*insert* active ingredient] may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include: • hives • facial swelling • asthma (wheezing) • shock • skin reddening • rash • blisters If an allergic reaction occurs, stop use and seek medical help right away. **Stomach bleeding warning:** This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you: • are age 60 or older • have had stomach ulcers or bleeding problems • take a blood thinning (anticoagulant) or steroid drug • take other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others] • have 3 or more alcoholic drinks every day while using this product • take more or for a longer time than directed
Do not use • if you have ever had an allergic reaction to any other pain reliever/fever reducer • right before or after heart surgery • with any other drug containing an NSAID (prescription or nonprescription). Ask a doctor or pharmacist before using with other drugs if you are not sure.
Ask a doctor before use if you have • problems or serious side effects from taking pain relievers or fever reducers • stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain • ulcers • bleeding problems • high blood pressure • heart or kidney disease • taken a diuretic • reached age 60 or older
Ask a doctor or pharmacist before use if you are • under a doctor's care for any serious condition • taking a blood thinning (anticoagulant) or steroid drug • taking any other drug
When using this product

• take with food or milk if stomach upset occurs • taking longer than 10 days or more than the recommended dose may increase the risk of heart attack or stroke
Stop use and ask a doctor if • you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding. • pain gets worse or lasts more than 10 days • fever gets worse or lasts more than 3 days • stomach pain or upset gets worse or lasts • redness or swelling is present in the painful area • any new symptoms appear
If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use [*NSAID active ingredient*] during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away.
Directions • **do not take more than directed** • **the smallest effective dose should be used** • do not take longer than 10 days, unless directed by a doctor (see Warnings) • **[add NDA approved direction]**
Other information • [storage conditions]
Inactive ingredients [list ingredients in alphabetical order]
Questions or comments? call **1-800-XXX-XXXX:** [insert appropriate times when the phone will be answered by a person, e.g., weekdays 8AM to 11 PM EST; weekends 9AM to 11 PM, EST]

PEDIATRIC DRUG FACTS LABEL:

Drug Facts

Active ingredient (in each [insert dosage unit]) ***Purpose***

Ibuprofen XXX mg (NSAID)*.....Pain reliever/fever reducer

* nonsteroidal anti-inflammatory drug

Uses

- [add NDA approved uses]

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include:

- hives
- facial swelling
- asthma (wheezing)
- shock
- skin reddening
- rash
- blisters

If an allergic reaction occurs, stop use and seek medical help right away.

Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if the user:

- has had stomach ulcers or bleeding problems
- takes a blood thinning (anticoagulant) or steroid drug
- takes other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others]
- takes more or for a longer time than directed
- has 3 or more alcoholic drinks every day while using this product
- is age 60 or older

Sore throat warning: Severe or persistent sore throat or sore throat accompanied by high fever, headache, nausea, and vomiting may be serious. Consult doctor promptly. Do not use more than 2 days or administer to children under 3 years of age unless directed by doctor.

Do not use

- if the user has ever had an allergic reaction to any other pain reliever/fever reducer
- right before or after heart surgery
- with any other drug containing an NSAID (prescription or nonprescription). Ask a doctor or pharmacist before using with other drugs if you are not sure.

Ask a doctor before use if the user has

- problems or serious side effects from taking pain relievers or fever reducers
- stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain
- ulcers
- bleeding problems
- not been drinking fluids
- lost a lot of fluid due to vomiting or diarrhea
- high blood pressure
- heart or kidney disease
- taken a diuretic
- reached age 60 or older

Ask a doctor or pharmacist before use if the user is • under a doctor's care for any serious condition • taking a blood thinning (anticoagulant) or steroid drug • taking any other drug
When using this product • take with food or milk if stomach upset occurs • taking longer than 10 days or more than the recommended dose may increase the risk of heart attack or stroke
Stop use and ask a doctor if • the user feels faint, vomits blood, or has bloody or black stools. These are signs of stomach bleeding. • stomach pain or upset gets worse or lasts • the user does not get any relief within first day (24 hours) of treatment • fever or pain gets worse or lasts more than 3 days • redness or swelling is present in the painful area • any new symptoms appear
If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use [*NSAID active ingredient*] during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away.
Directions • **do not give more than directed** • do not give longer than 10 days, unless directed by a doctor (see Warnings) • [add NDA approved directions]
Other information • [storage conditions]
Inactive ingredients [list ingredients in alphabetical order]
Questions or comments? call **1-800-XXX-XXXX:** [insert appropriate times when the phone will be answered by a person, e.g., weekdays 8AM to 11 PM EST; weekends 9AM to 11 PM, EST]

PRINCIPAL DISPLAY PANEL:

Proprietary Name (if used) Established name (**NSAID**), XXX mg Pain reliever/fever reducer

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

LASANDRA MADDEN Individually and on Behalf of LABREA WILLIAMS, a minor child,	§	
Plaintiffs,	§	
vs.	§	CIVIL ACTION NO. 3:03-CV-0167-BD
WYETH d/b/a WYETH, INC., f/k/a AMERICAN HOME PRODUCTS CORPORATION; WYETH CONSUMER HEALTHCARE, an unincorporated Division of WYETH, f/k/a WHITEHALL-ROBINS HEALTHCARE; AND WHITEHALL LABORATORIES, INC.,	§	
Defendants.	§	

AFFIDAVIT OF JAMES C. BARBER INSUPPORT OF PLAINTIFFS' REPLY TO DEFENDANT'S RESPONSE TO PLAINTIFFS' MOTION FOR PARTIAL SUMMARY JUDGMENT

STATE OF TEXAS)
)
COUNTY OF DALLAS)

BEFORE ME, the undersigned authority on this personally appeared James C. Barber, known by me to be the person whose signature appears below, and being duly sworn, stated that the following statement is true and correct:

1. "My name is James C. Barber, I am over 21 years of age, of sound mind, and capable of making this affidavit. I am plaintiffs' counsel in the above-entitled and numbered cause, and I am personally acquainted with the facts stated in this affidavit and they are all true and correct.

2. The following documents are contained in the Appendix to plaintiffs' Reply:

Att. 1 is a true and correct copy of a Letter from defense counsel Bill Sims dated April 22, 2005.

Att. 2 is true and correct copies of the FDA Supplemental Labeling Request dated June 15, 2005."

"Further affiant sayeth naught."

JAMES C. BARBER

SUBSCRIBED AND SWORN TO BEFORE ME on the 21st day of June, 2005, to certify which witness my hand and official seal.

Linda J Voyles
Notary Public in and for the
State of Texas

My Commission Expires: 11/03/08

Linda J. Voyles
Notary Public, State of Texas
My Comm. Expires 11/03/08